

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date  
15 September 2005 (15.09.2005)

PCT

(10) International Publication Number  
**WO 2005/084695 A2**

(51) International Patent Classification<sup>7</sup>: A61K 38/16

(21) International Application Number:  
PCT/GB2005/000751

(22) International Filing Date: 28 February 2005 (28.02.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0404487.1 28 February 2004 (28.02.2004) GB

(71) Applicant (for all designated States except US):  
PROTHERICS MOLECULAR DESIGN LIMITED [GB/GB]; The Health Business and Technical Park, Runcorn, Cheshire WA7 4QF (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): MELTON, Roger [GB/GB]; Morvus Technology Limited, Building 115,

Porton Down Science Park, Salisbury, Wiltshire SP4 0JG (GB). ATKINSON, Anthony [GB/GB]; Morvus Technology Limited, Building 115, Porton Down Science Park, Salisbury, Wiltshire SP4 0JG (GB).

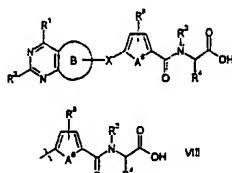
(74) Agent: MILES, John; Eric Potter Clarkson, Park View House, 58 The Ropewalk, Nottingham NG1 5DD (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

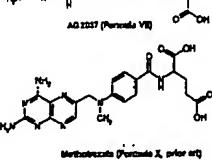
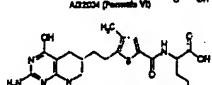
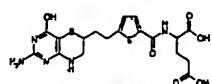
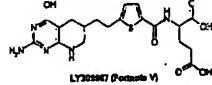
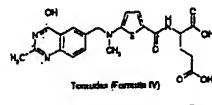
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH,

[Continued on next page]

(54) Title: USE OF ENZYME



(57) Abstract: A method of combating toxicity caused by an antifolate compound of Formula: (I), in an individual who has been administered the compound. The method comprises administering an enzyme that has carboxypeptidase G activity to the individual. A method of cleaving a compound comprising a structural fragment of Formula: (VIII), the method comprising contacting the compound comprising the structural fragment of Formula: (VIII) with an enzyme that has carboxypeptidase G activity.



WO 2005/084695 A2

BEST AVAILABLE COPY

WO 2005/084695 A2



GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,  
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished  
upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

BEST AVAILABLE COPY